IN THE CLAIMS:

Reinstate Claims 4-9, 14-17, 25, 29, 38, 44-61, 66-68, 70-73, 79-89 and 98-105; amend Claims 2, 4, 6, 14-17, 25, 29, 38, 47, 54, 56-58, 60, 61, 65, 66, 70, 74, 75, 77-89, 92, 94, 95 and 97-105; and cancel Claims 96, 106 and 107, as shown in the following listing:

1. (Cancelled)

2. (Currently Amended): A method of synthesizing a collection of polyamines, and polyamine vanadium or chromium complex compounds, which have one or more of the following recognized actions,

competitive inhibition of uptake of xenobiotics at the polyamine transport site, such organic molecules being a cause of DNA damage,

steric shielding of DNA from organic molecules by compacting DNA,

limitation of mitochondrial DNA damage by removal of free copper, iron and nickel ions by means of an aliphatic tetramine,

induction of metallothionein gene transcription,

induction of nerve growth factor, brain derived neuronotrophic factor and neuronotrophin-3 gene transcription,

regulation of affinity of NMDA receptors and blockade of the MK801 ion channel,

inhibition of protein kinase C,

mitochondrial reuptake of calcium,

binding and conservation of reduced glutathione,

induction of ornithine decarboxylase by glutathione,

maintenance of the homeostasis of the redox environment,

non toxic chelation of divalent metals in brain,

regulation of activity of pre-aspartate proteases,

inhibition of acetylcholinesterase and butyrylcholinesterase,

blockade of muscarinic M_2 receptors,

maintenance of ratio of membrane phosphtidylcholine to phosphatidylserine,

inhibition of superoxide dismutase, amine oxidase, and monoamine oxidase B,

regulation of brain polyamine levels in dementia with maintenance of endogenous polyamine levels,

stimulation of release of insulin by promoting exocytosis,

enhancement of glucose tolerance and decrease of blood cholesterol and triglycerides, and increase of high density lipoprotein,

decrease of P-enolpyruvate carboxykinase (PEPCK) transcription, thus decrease gluconeogenesis,

decrease of tyrosine aminotransferase gene expression,

increase of expression of glucokinase gene,

inducement of pyruvate kinase,

decrease in mitochondrial 3-hydroxy-3-methylglutaryl-CoA synthase (HMGCoAS) gene expression,

decrease in the expression of the liver and pancreas glucose-transporter GLUT-2 gene in diabetic animals to the level seen in controls,

increase in the amount of the insulin-sensitive glucose transporter, GLUT4 by stimulating its transcription,

inhibition of protein tyrosine phosphatases (PTP) u) suppressing nitric oxide production by macrophages,

positive cardiac inotropic effect,

restoration of albumin mRNA levels in diabetic animals by increasing hepatic nuclear factor 1 (HNF 1),

restoration of triiodothyronine T_3 levels, and

PPARα and PPARγ agonism or antagonism;

for use in the experimental treatment of degenerative diseases and mitochondrial genetic defects

~~treating degenerative diseases of the group consisting essentially of~~

~~Parkinson's disease,~~

~~Alzheimer's disease,~~

~~Lou Gehrig's disease,~~

~~Binswanger's disease,~~

~~Olivopontine Cerebellar Degeneration,~~

~~Lewy Body disease,~~

~~Diabetes,~~

~~Stroke,~~

~~Atherosclerosis,~~

~~Myocardial Ischemia,~~

~~Cardiomyopathy,~~

~~Nephropathy,~~

~~Ischemia,~~

~~Glaucoma,~~

~~Presbycussis, and~~

~~Cancer~~

~~due to acquired mitochondrial DNA damage,~~

~~redox damage to mitochondrial macromolecules~~

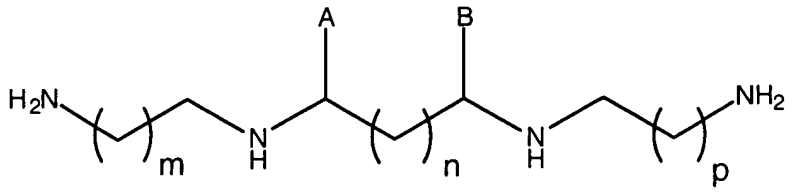
~~and inherited mitochondrial genetic defects~~

~~said method comprising the steps of: selecting a non superoxide dismutase mimic composition from a group consisting of non metallic polyamines, chromium polyamines and vanadium polyamines;~~

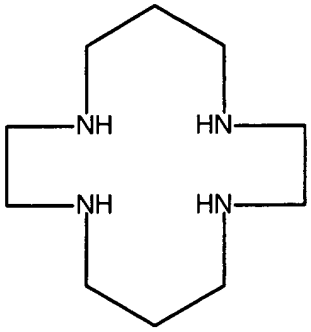
~~synthesizing said composition; and~~

~~administering an effective dose of said composition to a mammal;~~

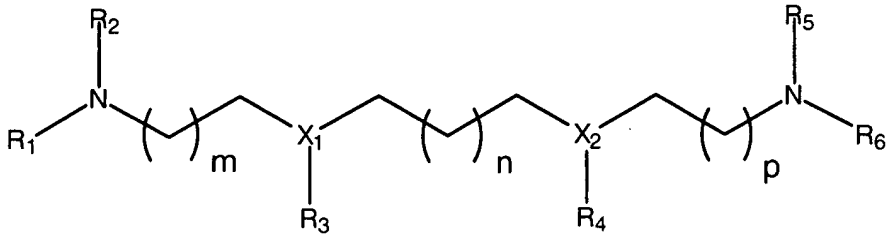
wherein said step of synthesizing comprises converting by treatment with an alkyl halide a compound taken from a group consisting of those compounds having the formula



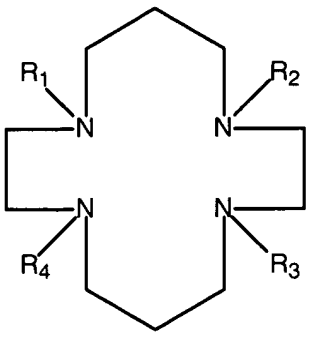
wherein A and B are hydrogen or alkyl, and m,n, and p are the same or different, and those compounds having the formula



3. (Previously presented): The method of claim 2 wherein said composition is taken from a group consisting of those compositions having the formulae:



and



wherein:

R_1 and R_2 are taken from a group consisting of hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol, α-lipoic acid, α-tocopherol, ubiquinone, phylloquinone, β-carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene, $-(CH_2)_n[XCH_2)_n]NH_2$ - wherein n = 3-6 and R_1 and R_2 taken together are $-(CH_2XCH_2)_n-$ wherein n = 3-6,

R_3 and R_4 are taken from a group consisting of hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol, α-lipoic acid, α-tocopherol, ubiquinone, phylloquinone, β-carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine , menaquinone, idebenone, dantrolene or heterocycle and R_3 and R_4 taken together are $-(CH_2XCH_2)_n-$ wherein n = 3-6,

R_5 and R_6 are taken from a group consisting of hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol, α-lipoic acid, α-tocopherol, ubiquinone, phylloquinone, β-carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene $-(CH_2)_n[XCH_2)_n]NH_2$ - wherein n = 3-6, and R_5 and R_6 taken together are $-(CH_2XCH_2)_n-$ wherein n = 3-6,

m, n, and p may be the same or different and are bridging groups of variable length from 3-12 carbons, and

X is taken from a group consisting of nitrogen, sulfur, phosporous and carbon.

4. (Reinstated and Currently Amended): The method of ~~Claim one~~ Claim 2 wherein said step of synthesizing further comprises the steps of:

-admixing an element taken from a group consisting of 2,4 dibromopropane and absolute ethanol into 1,2-diaminoethane hydrate;

-heating the resulting mixture to approximately 50^0C for about one hour;

-adding potassium chloride;

-continuing said heating for three hours;

-filtering potassium bromide out of the mixture;

-distilling the mixture at reduced pressure;

-allowing the formation of top and bottom layers;

-separating and distilling the top layer;

-converting free amine in the distilled top layer to a tetrahydrochloride salt; and

-converting said salt to a free amine by treatment with ammonium hydroxide.

5. (Reinstated): The method of claim 4 wherein said step of converting to a tetrahydrochloride salt comprises adding hydrochloric acid to said distilled top layer.

6. (Reinstated and Currently Amended): The method of Claim 4 wherein said ~~composition~~ compound consists of 1,3-bis-[(2'-aminoethyl)-amino]propane and step of admixing a solution comprises preparing said solution by mixing 1,3-dibromopropane and absolute ethanol in a ratio of approximately 1 to 3 per weight.

7. (Reinstated): The method of Claim 6 wherein said step of admixing further comprises slowly adding said solution into 1,2-diaminoethane hydrate in a ratio of approximately 2.6 to 1 per weight.

8. (Reinstated): The method of claim 7 wherein, the step of preparing said solution comprises mixing 15 grams of 1,3-diaminopropane and 50 milliliters of absolute ethanol; and
the step of slowly adding comprises adding said solution to 20 grams of potassium chloride;

9. (Reinstated): The method of Claim 8 wherein said step of converting to a tetrahydrochloride salt comprises adding six molar concentration of hydrochloric acid.

10.-13. (Canceled).

14. (Reinstated and Currently Amended): The method of ~~Claim 13~~ Claim 2 wherein ~~said degenerative diseases comprise neurodegenerative diseases characterized by excess iron pools and~~ said compound is selected from a group consisting of 2,2,2-piperidine and 2,3,2 adamantane.

15. (Reinstated and Currently Amended): The method of Claim 13 wherein ~~said degenerative diseases comprise ischemic damage and pump failure post myocardial infarction characterized by iron induced toxic redox effects and depletion of tissue zinc stores; and~~ said compound is selected from a group consisting of zinc cyclam methylated, zinc cyclam adamantane, cyclam methylated and cyclam adamantane.

16. (Reinstated and Currently Amended): The method of Claim 13 wherein said ~~degenerative diseases comprise neurodegenerative diseases and strokes; and said composition~~ compound is selected from a group consisting of compositions having open ring metal binding molecules taken from a group consisting of compositions having copper binding molecules and manganese binding molecules.

17. (Reinstated and Currently Amended): The method of Claim 16 wherein said compositions include compositions having copper-binding molecules include 2,3,2 isopropyl on N1/N4; and ~~said~~ compositions having manganese-binding molecules include 3,3,3 tetramine.

18.-24. (Canceled)

25. (Reinstated and Currently Amended): The method of ~~Claim 22~~ Claim 2 wherein said ~~degenerative disease comprises Alzheimer's disease and presbycussis; and said composition is derived from compounds~~ compound is selected from a group consisting of α lipoic acid and acetyl-l-carnitine polyamines.

26-28 (Canceled).

29. (Reinstated and Currently Amended): The method of ~~Claim 22~~ Claim 2 wherein said ~~degenerative diseases comprise cancer; and said composition~~ compound is taken from a group consisting of cobalt di-homocysteine polyamines.

30.-37. (Cancelled)

38. (Reinstated and Currently Amended): The method of ~~Claim 20~~ Claim 2 wherein; said compound ~~consisting~~ consists of pyridine tetramine.

39.-43. (Canceled)

44. (Reinstated): The method of Claim 4 wherein said composition consists of (2-aminoethyl){3-[(2-aminoethyl)amino]-1-methylbutyl}amine; and said step of admixing a solution comprises preparing said solution by mixing 2,4 dibromopropane and absolute ethanol in a ratio of approximately 1 to 20 per weight.

45. (Reinstated): The method of claim 44 wherein said step of admixing comprises slowly adding said solution into 1,2-diaminoethane hydrate in a ratio of approximately 44 to 1 per weight.

46. (Reinstated): The method of claim 45 wherein said step of converting to a tetrahydrochloride salt comprises of adding hydrochloric acid.

47. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of (2-aminoethyl){3-[(2-aminoethyl)amino]-1-methylbutyl}amine; and said step of synthesizing further comprises; the steps of

-admixing a solution of an element, taken from a group consisting of 1,3-diaminopropane and N,N-dimethyl-1,3-propanediamine and ethanol into 2-chloromethylpiperidine in water;

-adjusting the pH of the resulting mixture to 9 by addition of 10% sodium hydroxide;

-stirring the mixture at room temperature and maintaining the pH between 8 and 9 by addition of sodium hydroxide over 3 days;

-allowing solvents to evaporate; and

-extracting residues with CH_2Cl_2.

48. (Reinstated): The method of Claim 47 wherein said step of admixing a solution further comprises adding said solution into chloromethyl pyridine in water in a ratio of approximately 5 to 3 per weight wherein said chloromethylpyridine is diluted into water in a ratio of approximately 1 to 5 per weight.

49. (Reinstated): The method of claim 48 wherein said step of admixing a solution comprises preparing said solution in a ratio of approximately 1 to 50 per weight.

50. (Reinstated): The method of Claim 49 wherein said steps of synthesizing comprises synthesizing

(2-pyridylmethyl){3-[(2-pyridylmethyl)amino]propyl}amine; and

said step of admixing a solution further comprises preparing said solution by mixing 1,3-diaminopropane in water with ethanol.

51. (Reinstated): The method of claim 50 when said step of synthesizing further comprises synthesizing methyl(3-[methyl(2-pyridylmethyl)amino]propyl}(2-pyridylmethyl)amine; and said step of admixing a solution further comprises preparing said solution by mixing N,N-dimethyl-1,3 propanediamine in water with ethanol.

52. (Reinstated): The method of claim 2 wherein said step of synthesizing comprises the steps of a preparation by adding a first solution of 1,3 diaminopropane and absolute ethanol dropwise into a second solution of ethanol and an element taken from a group consisting of 1-(2chloroethyl)piperidine and 1-(2-chloroethylpiperizine) and admixing over approximately 30 minutes;

stirring said preparation over approximately 24 hours;

evaporating the solvents in said preparation;

extracting the residue using a volume of CH_2Cl_2 dried over Na_2SO_4 and evaporated to dryness;

purifying the resulting composition by converting to its hydrochloride salt by adding hydrochloric acid; and

converting said salt to its free amine by treatment with NH_4OH.

53. (Reinstated): The method of claim 52 wherein said step of mixing a preparation comprises

forming said first solution of 1,3 diaminopropane and ethanol in a ratio of approximately 1 to 100 per weight and adding said first solution into said second solution in a ratio of approximately 1 to 1 by weight.

54. (Reinstated and Currently Amended) The method of Claim 2 wherein said ~~composition~~ compound consists of

[2-(methylethylamino)ethyl](3-{[2-(methylamino)ethyl]amino}propyl)amine; and said step of synthesizing further comprises; preparing of first mixture of magnesium turnings,

1,3-bis-[(2'-aminoethyl)-amino]propane, benzene and acetyl chloride respective approximate percentage of 0.6%, 8.5%, 8.45%, and 6.4% per weight;

cooling said first mixture;

separating the mixture into a liquid phase and a solid phase;

preparing a second mixture by mixing said solid phase with ether;

preparing a solution by pouring said second mixture over ice;

preparing a third mixture by adding said solution to said liquid phase;

washing said third mixture with sodium bicarbonate;

washing said third mixture with water.

55. (Reinstated): The method of Claim 2 wherein said step of synthesizing comprises converting the starting di – or tetramine component, at least one of said components in said compounds to the corresponding N-substituted compound by treatment with an alkyl halide; and

purifying said composition by conversion to a salt through addition of hydrochloric acid.

56. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of (2-aminoethyl){3-[(2-aminoethyl)methylamino]propyl}methylamine, and

said step of synthesizing further comprises:

preparing a first solution of N,N-dimethyl-1,3-propanediamine and ethanol in a ratio of approximately 1 to 50 per weight;

preparing a second solution of 2-chloroethylamine and ethanol in a ratio of approximately 1 to 17 per weight;

combining said first and second solutions into a third solution;

stirring said third solution at room temperature for approximately 20 hours;

evaporating solvents in said third solution; and

extracting residues in said solution with a volume of CH_2Cl_2.

57. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of

[2-(bicyclo[3.3.1]non-3-ylamino)ethyl](3-{2-(bicyclo[3.3.1]non-3-ylamino)ethyl]amino}propyl)amine, and said step of synthesizing further comprises heating for approximately 6 hours at 215^0C a mixture of 1-bromoadamantane and 2,3,2-tetramine in a mol ratio of approximately 1 to 5;

admixing said mixture into a solution of 2NHCl and ether having a ratio of approximately 1.25 to 1 per weight, in a ratio of approximately 1 to 9 per weight;

separating the aqueous layer and alkalinizing said layer in a volume of 50% aqueous NaOH;

extracting with ether;

drying the extract over K_2CO_3; and

evaporating to an oil.

58. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of [2-(methylethylamino)ethyl](3 {[2-(methylamino)ethyl]amino}propyl)amine; and

said methylating step of synthesizing further comprises;

methylating terminal nitrogens of 2,3,2 tetramine by refluxing in the presence of benzene and acetyl chloride.

59. (Reinstated): The method of Claim 58 wherein said step of synthesizing further comprises;

preparing a first mixture of magnesium turnings;

of 1,3-bis-[(2'-aminoethyl)-amino]propane, benzene and acetyl chloride respective approximate percentage of 0.6%, 8.5%, 8.45%, and 6.4% per weight;

cooling said first mixture;

separating the mixture into a liquid phase and a solid phase;

preparing a second mixture by mixing said solid phase with ether;

preparing a solution by pouring said second mixture over ice;

preparing a third mixture by adding said solution to said liquid phase;

washing said third mixture with sodium bicarbonate;

washing said third mixture with water;

drying said third mixture over $CaCl_2$;

filtering said third mixture;

preparing a fourth mixture of said third mixture sodium hydride and N,N,-dimethylformamide in a ratio of approximately 2.5, 1 and 37.5 respectively per weight;

heating said fourth mixture under N_2 at approximately 60^0C for about three hours;

treating said fourth mixture with approximately ¼ its volume of iodomethane;

stirring said treated fourth mixture at 50^0C for approximately 24 hours;

quenching said treated fourth mixture with 95% ethanol;

removing volatiles at reduced pressure;

watering with addition of approximately ½ volume of water;

extracting organic products with approximately three ½ volumes of chloroform;

washing said organic products with water and NaCl;

drying said organic products over anhydrous sodium sulfate;

concentrating into an oil;

purifying said oil by flash chromatography with ¼ hexanes-ethyl acetate as eluent into an acetylated oil of said composition;

forming a solution of said acetylated oil, potassium hydroxide, methanol and water in respective proportions of 1, 3, 23 and 5 per weight respectively;

heating said solution under reflux for about 24 hours;

removing methanol at reduced pressure;

extracting into ether;

washing with NaCl;

drying over sodium sulfate;

concentrating under vacuum;

purifying by flash chromatography; and

evaporating solvents.

60. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of [2-(dimethylamino)ethyl](3-{[2-(dimethylamino)ethyl]methylamino}propyl)methylamine; and

said steps of synthesizing further comprises;

refluxing for about 20 hours a solution of 2,3,2 tetramine, formic acid and 37% formaldehyde and water in a weight proportions of approximately 1,10,10 and 1 respectively;

evaporating solvents from said solution;

making said solution basic by addition of NaOH; and

extracting residues with 3 times $1^1/_2$ volume of CH_2Cl_2.

61. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of 2-[3-(2-aminoethylthio)propylthio]ethylamine; and

said step of synthesizing further comprises:

preparing a first solution of 1,3-dimercaptopropane and water in a weight ration of about 1 to 50;

preparing a second solution of NaOH and water in a weight ratio of about 1.5 to 10;

forming a first mixture by mixing said first and second solutions in a weight ratio of about 5 to 1;

forming a third solution of 2-chloroethylamine and ethanol in a weight ratio of about 8.5 to 1;

admixing said solution into said mixture in a ratio of about 1 to 3.8;

refluxing said mixture over approximately 8 hours;

evaporating solvents from said refluxed mixture;

extracting residues with CH_2Cl_2.

62.-64. (Cancelled).

65. (Currently Amended): A method of Claim 2 ~~treating degenerative diseases of the group consisting essentially of~~

~~Parkinson's disease,~~

~~Alzheimer's disease,~~

~~Lou Gehrig's disease,~~

~~Binswanger's disease,~~

~~Olivopontine Cerebellar Degeneration,~~

~~Lewy Body disease,~~

~~Diabetes,~~

~~Stroke,~~

~~Atherosclerosis,~~

~~Myocardial Ischemia,~~

~~Cardiomyopathy,~~

~~Nephropathy,~~

~~Ischemia,~~

~~Glaucoma,~~

~~Presbycussis, and~~

~~Cancer~~

~~due to acquired mitochondrial DNA damage,~~

~~redox damage to mitochondrial macromolecules~~

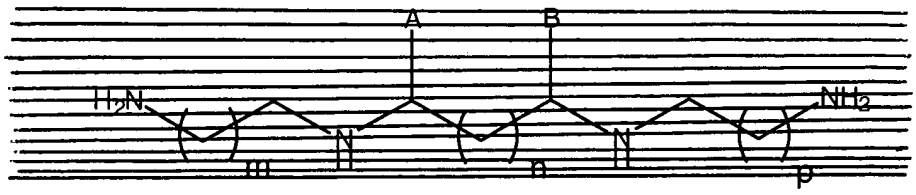
~~and inherited mitochondrial genetic defects~~

~~said method comprising the steps of: selecting a composition from a group consisting of open ring polyamines, macrocyclic polyamines, branched linear polyamines and substituted polyamines;~~

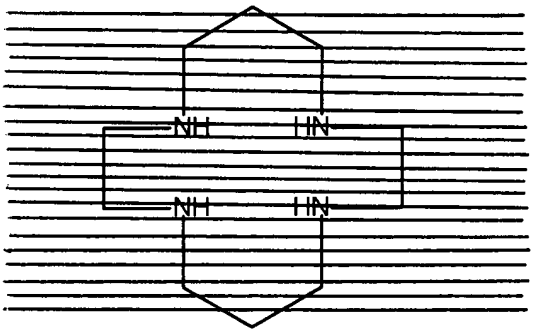
~~synthesizing said composition; and~~

~~administering an effective dose of said composition to a mammal;~~

~~wherein said step of synthesizing comprises converting by treatment with an alkyl halide a compound taken from a group consisting of those compounds having the formula~~



~~wherein A and B are hydrogen or alkyl, and m, n, and p are the same or different, and those compounds having the formula~~



wherein said composition consists of 1,4,8,11-tetraaza-1,4,8,11-tetraethylcyclotetradecane; and

said step of synthesizing further comprises:

forming a solution of cyclam and DMF in a weight ratio of approximately 1 to 50;

admixing under stirring small portions of NaH in a weight ratio of about 1 to 12.5;

heating said solution for about three hours at about 60^0C;

admixing iodoethane in a single portion into said solution in a weight ratio of about 1 to 17.5;

heating said solution at about 60^0C over about 18 hours;

quenching the solution with about 95% ethanol;

extracting residue with CH_2Cl_2.

66. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of N,N'-(2' dimethylphosphinoethyl)-propylenediamine; and the step of synthesizing further comprises:

incorporating phosphorus into a molecule of propylenediamine in place of two of its nitrogen atoms by addition and reduction reactions.

67. (Reinstated): The method of Claim 66 wherein said step of incorporating comprises:

preparing a first solution by dissolving propylenediamine into ethanol in a weight ratio of about 1 to 50;

admixing dimethylvinylphosphine sulfide into said solution in a weight ratio of about 1 to 22;

heating at reflux said solution for about 72 hours;

evaporating solvents under reduced pressure, leaving a residue.

68. (Reinstated): The method of Claim 67 wherein said step of incorporating further comprises:

dissolving said residue in chloroform;

washing said residue with NaOH; and

drying said residue over $MgSO_4$.

69. (Original): The method of Claim 68 wherein said step of synthesizing further comprises:

removing solvents in said residue under reduced pressure to yield an oil,

crystallizing said oil with ethyl acetate;

preparing a suspension of $LiAlH_4$ in dry dioxane in a weight ratio of about 1 to 100;

admixing said oil into said suspension;

to yield a mixture;

refluxing said mixture for about 36 hours;

cooling said mixture; and

adding a solution of dioxane in water and NaOH into said mixture.

70. (Reinstated and Currently Amended): The method of Claim 2 wherein ~~said diseases consist of diabetes and abnormal low density lipoprotein (LDL) to high density lipoprotein (HDL) ratio and~~ said composition is selected from a group consisting of vanadyl 2,3,2-tetramine and chromium 2,3,2-tetramine; and

said step of synthesizing further comprises reacting a metallic salt with 2,3,2-tetramine in an ethanol solution.

71. (Reinstated): The method of Claim 70 wherein said step of reacting comprises:

forming a first solution of 2,3,2 tetramine in ethanol in a weight ratio of about 1 to 20;

forming a second solution of vanadyl acetylacetonate in ethanol in a weight ratio of about 1 to 275;

admixing said second solution into said first solution in a volume ratio of about 1 to 1; and

refluxing said solution for almost 30 minutes.

72. (Reinstated): The method of Claim 70 wherein said step of reacting further comprises:

preparing a first solution of 2,3,2-tetramine in ethanol in a weight ratio of about 1 to 20;

preparing a second solution of chromium (III) nitrate in ethanol in a weight ratio of about 1 to 80;

admixing said second solution into said first solution in a volume ratio of about 1 to 1; and refluxing said solution for about 30 minutes.

73. (Reinstated): The method of Claim 55 wherein said step of converting comprises using amines to attach alkyl halide in a nucleophilic substitution of N atoms.

74. (Currently Amended): The method of Claim 3 wherein

said ~~step of selecting comprises selecting a~~ compound comprises a macrocyclic polyamine~~;~~

~~and~~

~~said diseases comprise diabetes and diabetes induced syndromes including congestive heart failure, myocardial infarction, stroke, glaucoma, atherosclerosis, cardiomyopathy, ischemia, optic neuropathy and peripheral neuropathy~~.

75. (Currently Amended): The method of claim 74 ~~wherein said step of selecting~~ which further comprises:

ascertaining the heats of formation of a set of macrocyclic polyamines; and choosing said compound in consideration of its heat of formation compared to the heats of formation of other compounds in said set.

76. (Previously presented): The method of claim 75 wherein: said step of ascertaining comprises: calculating the heats at the formation of said set of macrocyclic polyamines from their respective constituent atoms.

77. (Currently Amended): The method of claim 76 ~~wherein said step of choosing~~ which further comprises determining the stabilities of said set of macrocyclic polyamines as a function of their respective heats of formation;

wherein said stabilities are determined in inverse proportion to said respective heats of formation; and

whereby the relative stabilities of the set of macrocyclic polyamines are deemed indicative of ability to yield the most stable complex when reacted with a metal ion.

78. (Currently Amended): The method of Claim 77 ~~wherein said step of choosing~~ which further comprises ~~electing~~ synthesizing one of said polyamine compositions having a heat of formation indicating that said one of said polyamine compositions does not actively bind with said metal ion, and

wherein said metal ion is selected from a group consisting of copper ions, iron ions, and zinc ions.

79. (Reinstated and Currently Amended): The method of Claim 78 wherein ~~said degenerative diseases comprise ischemic damage and pump failure post myocardial infarction characterized by iron induced toxic redox effects and depletion of tissue zinc stores; and~~ said compound is selected from a group consisting of zinc cyclam methylated, zinc cyclam adamantane, cyclam methylated and cyclam adamantane.

80. (Reinstated and Currently Amended): The method of claim 78 wherein said ~~degenerative diseases comprise neurodegenerative disorders, stroke, glaucoma, atherosclerosis, cardiomyopathy, ischemia, optic neuropathy, peripheral neuropathy, presbycussis and cancer;~~

~~and said composition~~ compound is selected from derivatives of those compounds having the largest ring molecules.

81. (Reinstated and Currently Amended): The method of claim 80 wherein said ~~compounds~~ compound comprises a compound having the largest ring molecules includes 3,3,3 tetramine, cyclam adamantanes, cyclam 3,3,3 and compounds having alkyl substituted molecules.

82. (Reinstated and Currently Amended): The method of Claim 78 wherein ~~said degenerative diseases comprise Parkinson's, Lou Gehrig's, Binswanger's, and Lewy Body diseases, Olivopontine Cerebellar Degeneration, stroke, glaucoma and optic neuropathy; and~~

said composition is selected from a group of compositions having alkyl side chains.

83. (Reinstated and Currently Amended): The method of Claim 78 wherein ~~said degenerative diseases comprise neurodegenerative diseases, ischemia post myocardial infarction and atherosclerosis; and~~

said ~~composition~~ compound is selected from derivatives of compounds from a group consisting of piperidine, piperazine and adamantane.

84. (Reinstated and Currently Amended): The method of claim 3 wherein ~~said degenerative diseases comprise stroke, diabetic neuropathy, peripheral neuropathy, Alzheimer's disease, atherosclerosis, ischemia, diabetes, presbycussis, cardiomyopathy and congestive heart failure; and~~ said ~~composition~~ compound is derived from compounds having terminal nitrogen added molecule substitution with elements selected from a group consisting of glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E,

hydroxytoluene, carvidilol, α lipoic acid, tocopherols, ubiquinone, phylloquinone, carotenes, menadione, glutamate, succinate, acetyl-l-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene and phosporous.

85. (Reinstated and Currently Amended): The method of Claim 84 wherein ~~said degenerative disease comprises stroke; and~~ said ~~composition~~ compound consists of uric acid polyamine.

86. (Reinstated and Currently Amended): The method of Claim 84 wherein ~~said degenerative disease comprises diabetes; and~~ said ~~composition~~ compound is derived from ~~compounds~~ a compound selected from a group consisting of phosphorous, taurine, CoEnzyme Q, α lipoic acid, tocopherol, succinate, glutamate and acetyl-l-carnitine polyamines.

87. (Reinstated and Currently Amended): The method of Claim 84 wherein ~~said degenerative disease comprises atherosclerosis; and~~ said ~~composition~~ compound selected from a group consisting of tocopherol polyamine and coenzyme Q polyamine.

88. (Reinstated and Currently Amended): The method of Claim 84 wherein ~~said degenerative disease comprises ischemia; and~~
said ~~composition~~ compound is selected from a group consisting of tocopherol polyamine and coenzyme Q polyamine.

89. (Reinstated and Currently Amended): The method of Claim 84 wherein ~~said diseases comprise myocardial degeneration and congestive heart failure; and~~ said ~~composition~~ compound consists of coenzyme Q polyamine.

90. (Previously presented): The method of Claim 3 wherein said step of converting comprises adjusting the in vivo half life and pharmacokinetic properties of said composition by selective terminal nitrogen substitutions.

91. (Previously presented): The method of Claim 3 wherein said step of converting comprises adjusting the in vivo half life and pharmacokinetic properties of said composition by addition of side chains on amino or methylene groups.

92. (Currently Amended): The method of Claim 3 ~~wherein said step of selecting~~ which further comprises:

finding the octanol / water coefficients of partition of a series of said compounds; and

picking said compound in consideration of its octanol / water coefficient compared to the octanol water coefficients of other compounds in said series.

93. (Previously presented): The method of Claim 92 wherein said step of picking comprises determining the abilities of said series of compounds to pass through the intestinal, blood brain and blood retinal barriers as a function of their respective octanol / water coefficients; wherein said abilities are determined according to a distribution curve centered about 2 and having a useful range extending towards 0.5 and 4, the numbers being log values.

94. (Currently Amended): The method of Claim 3 ~~wherein said step of selecting~~ which further comprises;

measuring pKas of a list of said compounds; and

selecting said compound in consideration of its pKas compared to the pKa's of other compounds on the list.

95. (Currently Amended): The method of Claim 94 ~~wherein said step of selecting~~ which further comprises;

selecting a composition with higher pKas ~~in the treatment a disease characterized by lower tissue pH~~ .

96. (Canceled).

97. (Currently Amended): The method of Claim 3 ~~wherein said step of selecting~~ which further comprises determining the respective likely efficiency of said ~~compounds~~ compound in consideration of the disease target to be treated and the route of administration.

98. (Reinstated and Currently Amended): The method of Claim 82 wherein ~~said degenerative disease consists of Alzheimer's disease and diabetes; and~~

said compound comprises acetyl-l-carnitine polyamine.

99. (Reinstated and Currently Amended): The method of Claim 84 wherein ~~said degenerative disease consists of diabetes; and~~

said ~~compounds are~~ compound is selected from a group consisting of 2,3,2 piperidine, glutamate polyamine, succinate polyamine, chromium tetramine and vanadyl tetramine and phosphorous polyamine.

100. (Reinstated and Currently Amended): The method of Claim 3 wherein ~~said degenerative diseases comprise peripheral neuropathy and optic neuropathy; and~~

said ~~compounds comprise~~ compound comprises taurine polyamine and ~~α~~ lipoic acid polyamines.

101. (Reinstated and Currently Amended): The method of Claim 3 wherein ~~said degenerative diseases comprise glaucoma; and said compounds comprise~~ said compound comprises adamantane 2,3,2 tetramine and adamantane cyclam.

102. (Reinstated and Currently Amended): The method of Claim 3 wherein ~~said degenerative disease comprise presbycussis; and said compounds comprise~~ said compound comprises α lipoic acid polyamine and acetyl-l-carnitine polyamine.

103. (Reinstated and Currently Amended): The method of Claim 3 wherein said ~~composition~~ compound consists of:

1,4,8,11-tetraaza-1,4,8,11-tetramethylcyclotetradecane; and

said steps of synthesizing comprises:

refluxing for about 18 hours a solution of cyclam, formic acid, 37% formaldehyde and water in weight proportions of approximately 1, 5.3, 4.5 and 1 respectively;

adding water to said solution in a weight ratio of approximately 0.5 to 1;

cooling said solution to about 5^0C;

adjust the pH of said solution to above 12 with NaOH;

extracting the solution with CH_2Cl_2.

104. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of 1,4,8,11-tetraaza-1,4,8,11-tetra(2-piperidylethyl)cyclotetradecane; and said step of synthesizing further comprises:

preparing a first solution of cyclam and CH_2Cl_2 in a weight ratio of approximately 1 to 50;

preparing a second solution of NaOH and water in a weight ratio of approximately 1 to 31;

preparing a mixture of said first and second solution in a weight ratio of approximately 1 to 1;

preparing a third solution of 1-(2-chloroethyl)piperidine and CH_2Cl_2 in a weight ratio of approximately 1 to 14;

adding said third solution dropwise into said mixture in a weight ratio of about 1 to 2;

stirring said mixture over about 24 hours;

evaporating solvents; and

extracting residues with CH_2Cl_2.

105. (Reinstated and Currently Amended): The method of Claim 2 wherein said ~~composition~~ compound consists of 1,4,8,11-tetraaza-1,4,8,11 -tetrabicyclo[3.3.1]non-3-ylcyclotetradecane; and

said step of synthesizing further comprises:

forming a first solution of cyclam and ethanol in a weight ratio of approximately 1 to 100;

forming a second solution of 1-bromoadamantane and ethanol in a weight ratio of 1 to 23;

forming a mixture by adding said second solution dropwise into said first solution in a weight ratio of about 1 to 1, over 30 minutes;

heating said mixture to reflux over about 20 hours;

evaporating said solution under reduced pressure; and

extracting residue from said solution with CH_2Cl_2.

106. (Canceled).

107. (Canceled).